Second-Generation Antipsychotic Agents: A Classic P&T Committee Dilemma

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By now, most readers know that I am not a psychiatrist! I was intrigued to read about a recent consensus development conference on the use of antipsychotic drugs and the development of obesity and diabetes—frankly, a connection that I had not realized.

Earlier this year, a number of reputable national organizations, including the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity, published a statement in the peer-reviewed journal, *Diabetes Care.* Let me share with you some of the major points from this important consensus development statement.

Antipsychotic medications are the mainstay of therapy for psychotic illness, and they are also widely available and very effective in treating many other psychiatric conditions, such as bipolar depression. These medications have been on the scene for more than 50 years and have helped millions of people not only in managing their symptoms but also in helping them return to productive lives. As I understand it, the so-called *first-generation* antipsychotics (FGAs) are, of course, still widely available and very effective in treating some of the key symptoms such as hallucinations and delusions.

Newer products, sometimes called “atypical antipsychotics,” or *second-generation* antipsychotics (SGAs), have been found to be more useful, producing fewer and less severe side effects. These newer medications are also more helpful in treating what psychiatrists call the “negative” symptoms of psychoses: withdrawal, apathy, lack of speech, and cognitive impairment.

Many P&T committee members probably know that six such SGAs are currently available, yet they vary greatly in their efficacy, formulation, biochemistry, receptor binding, and side-effect profiles. Although they are better tolerated and generally thought to be more effective than the older agents, the question remains: which ones should we choose to put on our formulary? Now the story gets more interesting.

Most SGAs carry a risk of diabetes and obesity when they are used to treat psychoses. Is this part of the overall picture of these diseases? Is there a greater prevalence of diabetes and obesity in this population to begin with? Nobody seems to be sure; however, it is clear that drugs such as risperidone (Risperdal®, Janssen), olanzapine (Zyprexa®, Eli Lilly) and quetiapine fumarate (Seroquel®, AstraZeneca) have been studied and cited as the causes of metabolic abnormalities, including weight gain, an increased risk for diabetes, and a worsening lipid profile, especially in terms of elevated low-density lipoprotein cholesterol (LDL-C) levels.

So far, two newer SGAs, ziprasidone (Geodon®, Pfizer) and aripiprazole (Abilify®, Bristol-Myers Squibb), appear to carry a lower risk of weight gain, diabetes, and LDL-C elevations.

Thus, we have a classic dilemma for P&T committees—a relatively new class of drugs with proven clinical efficacy but a complex side-effect profile. The consensus development report concludes with this statement:

These adverse conditions are closely linked, and their prevalence appears to differ depending on the SGA used. Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate effects. Aripiprazole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as the other agents.

What is a P&T committee member to do? Again, although I am not trained in psychiatry, I know when it is important to take a stand regarding drug efficacy and the impact of a side-effect profile. I surely hope that all P&T committee members understand these important, but sometimes subtle, differences in this class of drugs and that they are making informed decisions.

Patients with psychoses are a challenge for all caregivers. It is our responsibility to help the treatment team by having these drugs available and by understanding their appropriate use. Consensus development statements like the one discussed here can go a long way toward sorting out these challenges.

As usual, I am interested in your views. You can reach me at my e-mail address, david.nash@jefferson.edu.

**REFERENCE**


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